

Amendment  
Application No. 08/853,870

Attorney Docket No. 23164-1001  
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administration of interferon for treating neoplastic disease and, thus, provides the motivation for the claimed methods. Applicant respectfully disagrees.

The present invention is directed towards a method of treatment of a neoplastic disease sensitive to interferon using ultra-high dose interferon. The Examiner has asserted that Sato et al. teaches the use of high dose interferon in the treatment of recurrent carcinoma, specifically pointing to Section 3 of the Clinical Tests (column 7, lines 35-52). Applicant respectfully disagrees that Sato fails to teaches such a method. The methods discussed in Sato are methods of treating keratotic disorders of the skin, such as lichen planus and leukoplakia, and not methods of treating cancer.

While the word "tumor" is used by Sato, a detailed examination of Sato shows that Sato's use of the word is not as a synonym for neoplasm. "Tumor" has a primary definition of "any swelling or tumefaction," with tumefaction being further defined as "a swelling." Stedman's Medical Dictionary, 26th edition, page 1870 - 1871 (copies enclosed). In sections 4 (column 7, lines 58-60) and 5 (column 8, lines 5-8) of the Clinical Tests, both dealing with leukoplakia, Sato uses the word "tumor" without a carcinoma being present. Substituting "swelling" for "tumor," the passage describes a characteristic of both lichen planus and leukoplakia, i.e., bumps, ridges or thickening of the skin or mucosa, and not of a neoplasm.

Sato may administer interferon to the oral cavity; however, Sato is not treating a carcinoma but rather lichen planus of the oral cavity. As a first indication that a carcinoma is not being treated, Section 3 of the Clinical Tests is labeled "Treatment of lichen planus." Furthermore, the introductory sentence of Section 3 (Column 7, lines 37-39) describes the treatment of the carcinoma as being effected by "primary focus excision and upper radical neck lymphnode dissection." Thus, the treatment for the carcinoma was surgery, not interferon administration. Subsequent to the surgical removal of the carcinoma lichen planus was observed and treated with interferon.

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Lichen planus is a skin disease of unknown origin and is not a form of cancer. Applicant respectfully submits a printout from an on-line pamphlet from the American Academy of Dermatology wherein it is acknowledged that lichen planus is not a neoplastic disease. See section labeled "What the disease is not" on page 1 (the information may also be accessed at <http://www.aad.org/aadpamphrework/lichen.htm>). Oral lichen planus is characterized by patches of fine white lines and dots, severe cases can cause painful sores and ulcers. Often a biopsy is needed to confirm a diagnosis of lichen planus. Similarly, leukoplakia is a keratotic skin disease characterized by a thickened area in the delicate lining of the mouth or tongue. The thickening is due to the deposition of keratin and may have a rough or bumpy appearance. Although leukoplakia may be premalignant, it is not a cancer. Thus, although leukoplakia and lichen planus have the characteristic of having bumps or minute swellings associated with their appearance, neither is a neoplasm.

Taken as a whole, Sato fails to provide motivation to one skilled in the art to treat a neoplastic disease with ultra-high dose interferon. Nowhere in the specification is the treatment of a carcinoma with interferon described or suggested. The Abstract, Summary, and Detailed Explanation are devoid of description of interferon treatment of a neoplastic disease. More telling is the fact that the Claims fail to claim the treatment of a carcinoma with ultra-high dose interferon; the Claims are directed to only treating lichen planus or leukoplakia. Thus, Sato can not be viewed as the treatment of a neoplastic disease by ultra-high dose interferon and fails to render obvious the present invention. Withdrawal of this rejection is respectfully requested.

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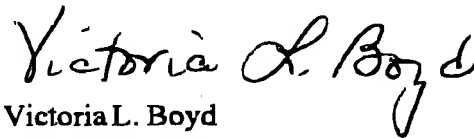
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Conclusion

The instant invention is directed to an ultra-high dose oromucosal interferon treatment, free of adverse reactions, of a neoplastic disease. The prior art fails to suggest or teach such a use of ultra-high dose oromucosal interferon. Further, there is no suggestion by Sato that interferon could be used in the treatment of a neoplastic disease.

All rejections having been addressed, reconsideration of the application in view of the foregoing remarks, and an early indication of allowability of Claim 6, 13, and 17 - 33 are earnestly solicited.

Respectfully submitted,



Victoria L. Boyd  
Attorney for Applicants  
Reg. No. 43,510

Date: September 10, 1999

Heller Ehrman White & McAuliffe  
525 University Avenue  
Palo Alto, CA 94301-1900  
(650) 324-7112

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## **Lichen Planus**

Lichen Planus (pronounced LY-kin-PLAN-us) is a rather uncommon skin disease. It affects about one percent of the general population. What is lichen planus? How do you get the disease? Can it be cured? This brochure will help answer these questions and more by taking a closer look at the disease.

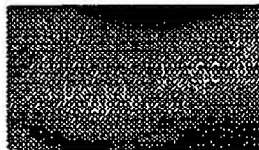
### **What the disease is not**

To understand what lichen planus (LP) is, it's important to note what the disease is not. Lichen planus is not an infectious disease. It is impossible to "catch" from someone who has it or give it to someone else. The disease is not a form of cancer. It does not appear to be inherited and is not nutrition related.

### **What it is**

Lichen planus is an inflammatory disease that strikes primarily the skin and mucous membranes. In rare cases, it also affects the hair and nails. The causes of lichen planus are largely unknown. A few cases are linked to allergic reactions to specific drugs or dental materials. It affects men and women equally, and occurs most often in middle-aged adults.

### **Lichen Planus of the Skin**



**Lichen planus on the wrist**

Lichen planus of the skin can be quite bothersome. The rash is characterized by reddish-purple, flat-topped bumps that are usually very itchy. They can be anywhere on the body, but seem to favor the inside of the wrists and ankles. The disease can also occur on the lower back, neck, genitals and in rare cases, the hair and nails. Thick patches may occur, especially on the shins. Blisters are rare. While the appearance of lichen planus makes the disease somewhat easy to identify, a skin biopsy may be needed to confirm its diagnosis.

**Specifics** About 20 percent of the time, lichen planus of the skin causes minimal symptoms and needs no treatment. However, in many cases there is severe itching. The cause of skin lichen planus is not known. There are cases of lichen planus - like allergic reactions to

► **Lichen Planus of the Mouth**

► **Are You at Risk?**

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known. There are cases of lichen planus - like allergic reactions to high blood pressure, heart disease and arthritis medications. In those cases, identifying and stopping use of the drug helps clear up the rash within a few weeks.

Most cases of lichen planus go away within two years. As it heals, lichen planus often leaves a dark brown discoloration on the skin. Like the bumps themselves, these stains may eventually fade with time without treatment. About one out of five people will have a second attack of lichen planus.

**Treatment Tactics** There is no known cure for skin lichen planus but treatment is often effective in relieving itching and improving the appearance of the rash until it goes away. Since every case of lichen planus is different, no one treatment does the job. The two most common methods include the use of topical corticosteroid creams and antihistamine drugs taken by mouth. Both work to help lessen inflammation and itching. More severe cases of lichen planus may require stronger medications such as cortisone taken internally or a specific form of ultraviolet light treatment called PUVA. Remember to discuss any potential drug side effects with your dermatologist prior to filling prescriptions.

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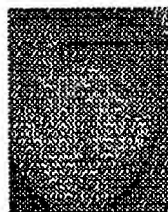


**Lichen planus on the ankles**

As with other skin disorders, patience - and following your doctor's advice - is the best medicine for dealing with lichen planus. You should, however, be careful not to injure your skin, since it could cause new areas of lichen planus to form in the damaged skin.

### **Lichen Planus of the Mouth**

Lichen planus of the mouth most commonly affects the inside of the cheeks, gums and tongue. Oral lichen planus is more difficult to treat and typically lasts longer than skin lichen planus. Fortunately, most cases of lichen planus of the mouth cause minimal problems. About a third of all people who have oral lichen planus also have skin lichen planus. Women may also have lichen planus of the vaginal area.



**The smooth white patches on the tongue are lichen planus**

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**Lichen planus of the gums produces redness and yellowish ulcerations.**

## Are You at Risk?

## Food for Thought

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Spicy foods, citrus juices, tomato products, caffeinated drinks like coffee and cola, and crispy foods like toast and corn chips should be decreased or eliminated from the diet as they can aggravate lichen planus and interfere with its ability to heal.

**Nail Involvement** Nail changes have been reported in about 10 percent of lichen planus cases. The majority of nail changes result from damage to the nail matrix, or nail root. Usually only a few fingernails or toenails are involved, but occasionally all are affected. Nail changes associated with lichen planus include longitudinal ridging and grooving, splitting, nail thinning and nail loss. In severe cases, the nail may be temporarily or permanently destroyed.



**Lichen planus affecting the fingernails shows thinning and surface roughness of the nail plate with longitudinal ridges.**

**Hair Involvement**



**Lichen planus of the scalp causes inflammation, hair loss and scarring.**

In rare cases, lichen planus can affect hairy areas. This is called lichen planopilaris, and can lead to inflammation, and in some cases, permanent hair loss.

**More on Lichen Planus**

Lichen planus is a stable condition - the severity and distribution of the disease rarely changes after the first two months. While there are many theories to explain lichen planus, many dermatologists believe it can be classified as an autoimmune disease. This means the inflammatory cells that normally fight germs attack normal parts of the skin, mucous membranes, hair and nails.

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## Symptoms, Illness & Surgery

Complete Guide to Symptoms, Illness, & Surgery

### LEUKOPLAKIA



#### Definition

#### General Information

A thickened area in the delicate lining of the mouth or tongue. This is not contagious, but it may be premalignant.

#### Body Parts Involved

Inside of cheek; floor of mouth; tongue; palate; roof of mouth.

#### Sex or Age Most Affected

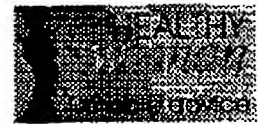
All ages, but most common in adults over 60.

#### Signs & Symptoms

- Sensitivity to hot and spicy food.
- A small white patch in the mouth. The patch feels firm, rough and stiff.
- No symptoms in the early stages.

#### Causes

- Some are unknown; others include:
- Deficiency of vitamins A or B.
  - Deficiency of male or female hormones.
  - Syphilis.
  - Chronic irritation in the mouth. The irritation may be from jagged teeth, ill-fitting dentures, hot or spicy food, excess



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**Risk Increases  
With**

alcohol consumption or  
nicotine.

- ✦ Use of tobacco products, including cigarettes, chewing tobacco, snuff, pipe or cigars.
- ✦ Dentures.
- ✦ Repeated or chronic trauma to oral regions (biting inside of cheek or lip).
- ✦ Alcohol consumption.

**How to Prevent**

- ✦ Don't smoke or use tobacco products.
- ✦ Inspect the mouth regularly if you wear dentures or smoke.
- ✦ Decrease consumption of hot or highly seasoned foods if suspicious lesions develop.
- ✦ Avoid alcohol.



**Diagnostic  
Measures**

- ✦ Your own observation of symptoms.
- ✦ Medical history and physical exam by a doctor or dentist.
- ✦ Biopsy .

**Appropriate Health  
Care**

- ✦ Doctor's treatment.
- ✦ Surgery to remove the lesions.
- ✦ Patches may be surgically removed (cryosurgery) using a local anesthetic.

**Possible  
Complications**

- ✦ The lesion may become cancerous if untreated (about 5% of patients).
- ✦ New lesions may develop after treatment.

**Probable Outcome**

Sometimes curable with removal of the source of irritation (such as tobacco) or with surgery.



**How to Treat**

**General Measures**

- ✦ Any recognizable irritation should be corrected or removed. Eliminate tobacco and alcohol (including alcoholic mouthwashes). Lesions may clear up after these factors are removed.
- ✦ Following surgery or biopsy: If bleeding occurs, press cotton gauze gently for 5 minutes against the operation site. 24 hours after the operation, rinse the mouth with a warm salt-water solution. Use 1/2 teaspoon salt in 8 oz. warm water. Repeat every 1 or 2 hours. Brush and floss teeth often and use antiseptic mouthwash during the healing process. A clean mouth heals faster.

**Medication**

- ✦ For minor pain, you may use non-prescription drugs such as acetaminophen.
- ✦ Your doctor may prescribe topical or oral forms of vitamin A (sometimes).

**Activity**

No restrictions.

**Diet**

Liquid or soft diet for 24 hours; then no special diet.

**Call Your Doctor If**

- ✦ You have symptoms of leukoplakia.
- ✦ The following occurs after surgery: Bleeding after 12 hours or more. Severe pain.

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## TUMOR

**tumor** (tū'mŏr). 1. Any swelling or tumefaction. 2. **syn** neoplasm. 3. One of the four signs of inflammation (t., calor, dolor, rubor) enunciated by Celsus. [*L. tumor*, a swelling]

**acinar cell t.**, a solid and cystic t. of the pancreas, occurring in young women; t. cells contain zymogen granules.

**acute splenic t.**, acute splenitis, enlargement, and softening of the spleen, usually due to bacteremia or severe bacterial toxemia.

**adenoid t.**, adenoma. or neoplasm with glandlike spaces.

**adenomatoid t.**, a small benign t. of the male epididymis and female genital tract, consisting of fibrous tissue or smooth muscle enclosing anastomosing glandlike spaces containing acid mucopolysaccharide lined by flattened cells that have ultra-structural characteristics of mesothelial cells. **syn** adenofibromyoma.

**adenoleiomyofibroma**, angiomaoid t., benign mesothelioma of genital tract, Recklinghausen's t.

**adenomatoid odontogenic t.**, a benign epithelial odontogenic t. appearing radiographically as a well-circumscribed radiolucent-radiopaque lesion usually surrounding the crown of an impacted tooth in an adolescent or young adult; characterized histologically by columnar cells organized in a duct-like configuration interspersed with spindle-shaped cells and amyloid-like deposition that gradually undergoes dystrophic calcification. **syn** adenameloblastoma, ameloblastic adenomatoid t.

**adipose t.**, **syn** lipoma.

**ameloblastic adenomatoid t.**, **syn** adenomatoid odontogenic t.

**amyloid t.**, **syn** nodular amyloidosis.

**angiomatoid t.**, **syn** adenomatoid t.

**aortic body t.**, **syn** chemodectoma.

**Bednar t.**, **syn** pigmented dermatofibrosarcoma protuberans.

**benign t.**, a t. that does not form metastases and does not invade and destroy adjacent normal tissue. **syn** innocent t.

**blood t.**, term sometimes used to denote an aneurysm, hemorrhagic cyst, or hematoma.

**borderline t.**, a neoplasm of the ovary, usually arising in young women, composed of complex epithelial hyperplasia without stromas invasion; may recur if incompletely removed surgically. but is clinically less aggressive than carcinoma. **syn** low malignant potential t.

**Brenner t.**, a relatively infrequent benign neoplasm of the ovary, consisting chiefly of fibrous tissue that contains nests of cells resembling transitional type epithelium, as well as glandlike structures that contain mucin; origin is controversial, but it may arise from Walther's cell rest; ordinarily found incidentally in ovaries removed for other reasons, especially in postmenopausal women.

**Brooke's t.**, **syn** trichoepithelioma.

**brown t.**, a mass of fibrous tissue containing hemosiderin-pigmented macrophages and multinucleated giant cells, replacing and expanding part of a bone in primary hyperparathyroidism.

**t. burden**, The total mass of tumor tissue carried by a patient with cancer.

**Buschke-Löwenstein t.**, **syn** giant condyloma.

**calcifying epithelial odontogenic t.**, a benign epithelial odontogenic neoplasm derived from the stratum intermedium of the enamel organ; a painless, slowly growing, mixed radiolucent-radiopaque lesion characterized histologically by cords of polyhedral epithelial cells, deposits of amyloid, and spherical calcifications. **syn** Pindborg t.

**carcinoid t.**, a usually small, slow-growing neoplasm composed of islands of rounded, oxyphilic, or spindle-shaped cells of medium size, with moderately small vesicular nuclei, and covered by intact mucosa with a yellow cut surface; neoplastic cells are frequently palisaded at the periphery of the small groups, and the latter have a tendency to infiltrate surrounding tissue. Such neoplasms occur anywhere in the gastrointestinal tract (and in the lungs and other sites), with approximately 90% in the appendix and the remainder chiefly in the ileum, but also in the stomach,

other parts of the small intestine, the colon, and the rectum; those of the appendix and small t.'s seldom metastasize, but reported incidences of metastases from other primary sites and from t.'s exceeding 2.0 cm in diameter vary from 25 to 75%; lymph nodes in the abdomen and the liver may be conspicuously involved, but metastases above the diaphragm are rare. **see** ALSO carcinoid syndrome. **syn** argentaffinoma.

**carotid body t.**, **syn** chemodectoma.

**cellular t.**, a t. composed mainly of closely packed cells.

**cerebellopontine angle t.**, **syn** acoustic schwannoma.

**chemoreceptor t.**, **syn** chemodectoma.

**chromaffin t.**, **syn** chromaffinoma.

**Codman's t.**, chondroblastoma of the proximal humerus.

**collision t.**, two originally separate t.'s, especially a carcinoma and a sarcoma, that appear to have developed by chance in close proximity, so that an area of mingling exists. **see** ALSO carcinosarcoma.

**connective t.**, any t. of the connective tissue group, such as osteoma, fibroma, sarcoma.

**dermal duct t.**, a benign small t. derived from the intradermal part of eccrine sweat gland ducts occurring often on the head and neck.

**dermoid t.**, **syn** dermoid cyst.

**desmoid t.**, **syn** desmoid (2).

**dysembryoplastic neuroepithelial t.**, a rare low grade neoplasm most frequently seen in children and associated with seizures and cortical dysplasia; the often multinodular, multicystic t. is comprised of an oligodendroglial-like background with accompanying neurons.

**eighth nerve t.**, **syn** acoustic schwannoma.

**embryonal t.**, **embryonic t.**, a neoplasm, usually malignant, which arises during intrauterine or early postnatal development from an organ rudiment or immature tissue; it forms immature structures characteristic of the part from which it arises, and may form other tissues as well. The term includes neuroblastoma and Wilms' t., and is also used to include certain neoplasms presenting in later life, this usage being based on the belief that such t.'s arise from embryonic rests. **see** ALSO teratoma. **syn** embryoma.

**embryonal t. of ciliary body**, **syn** embryonal medulloepithelioma.

**endocervical sinus t.**, malignant germ cell t. commonly found in the ovary. The t. arises from primitive germ cells and develops into extra-embryonic tissue resembling the yolk sac. **syn** yolk sac carcinoma.

**endodermal sinus t.**, a malignant neoplasm occurring in the gonads, in sacrococcygeal teratomas, and in the mediastinum; produces  $\alpha$ -fetoprotein and is thought to be derived from primitive endodermal cells. **syn** yolk sac t.

**endometrioid t.**, a t. of the ovary containing epithelial or stromal elements resembling t.'s of the endometrium.

**Erdheim t.**, **syn** craniopharyngioma.

**Ewing's t.**, a malignant neoplasm which occurs usually before the age of 20 years, about twice as frequently in males, and in about 75% of patients involves bones of the extremities, including the shoulder girdle, with a predilection for the metaphysis; histologically, there are conspicuous foci of necrosis in association with irregular masses of small, regular, rounded, or ovoid cells (2 to 3 times the diameter of erythrocytes), with very scanty cytoplasm. **syn** endothelial myeloma, Ewing's sarcoma.

**fecal t.**, **syn** coproma.

**fibroid t.**, old term for certain fibromas and leiomyomas.

**giant cell t. of bone**, a soft, reddish brown, sometimes malignant, osteolytic t. composed of multinucleated giant cells and ovoid or spindle-shaped cells, occurring most frequently in an end of a long tubular bone of young adults. **syn** giant cell myeloma, osteoclastoma.

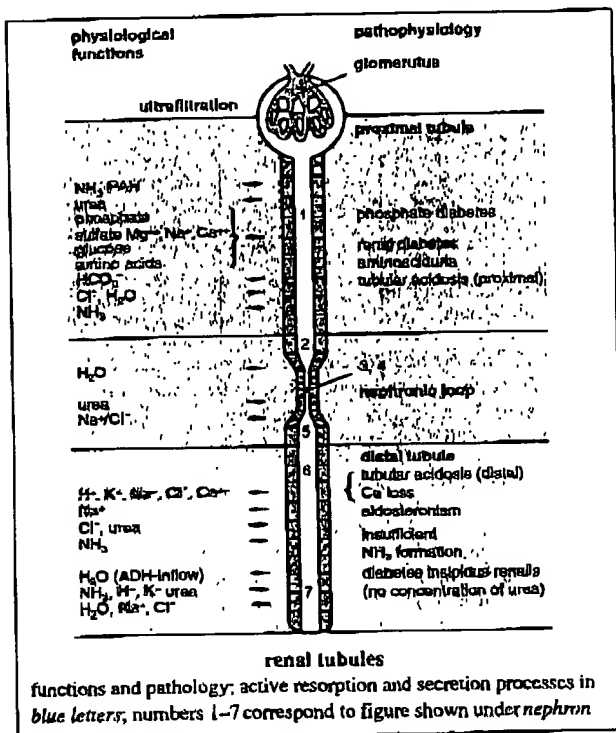
**giant cell t. of tendon sheath**, a nodule, possibly inflammatory in nature, arising commonly from the flexor sheath of the fingers and thumb; composed of fibrous tissue, lipid- and hemosiderin-containing macrophages, and multinucleated giant cells. **syn** localized nodular tenosynovitis.

**glomus t.** [MIM\*138000], an unusual vascular neoplasm composed of specialized pericytes (sometimes termed glomus cells),

## tubulization

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tumid



of some slowly absorbable material to keep the surrounding tissues from pushing in and preventing union.

**tu-bu-lo-cyst** (tū'byū-lō-sist). A cyst formed by the dilation of any occluded canal or tube. SYN tubular cyst.

**tu-bu-lo-der-moid** (tū'byū-lō-der'moyd). A dermoid cyst arising from a persistent embryonal tubular structure.

**tu-bu-lo-neo-gen-e-sis** (tū'byū-lō-nē'ō-jen'ē-sis). The formation of new tubules; usually refers to proliferation of tubules in renal tumors such as Wilms' tumor or mesoblastic nephroma. [tubule + neogenesis]

**tu-bu-lo-rac-e-mose** (tū'byū-lō-ras'ē-mōs). Denoting a gland of combined tubular and racemose structure.

**tu-bu-lor-rhex-is** (tū'byū-lō-rek'sis). A pathologic process characterized by necrosis of the epithelial lining in localized segments of renal tubules, with focal rupture or loss of the basement membrane. [tubule + G. *rhexis*, a breaking]

**tu-bu-lose**, **tu-bu-lous** (tū'byū-lōs, -lōs). Having many tubules.

**tu-bu-lus**, pl. **tu-bu-li** (tū'byū-lōs, -lī). SYN tubule. [L. dim. of *tubus*, a pipe]

**tu'buli bilif'eri**, SYN biliary ductules, under *ductule*.

**t. contor'tus**, (1) SYN convoluted tubule of kidney. (2) SYN convoluted seminiferous tubule.

**tu'buli dent'a'les**, SYN canaliculi dentales, under *canaliculus*.

**tu'buli epo'ph'ori**, SYN transverse ductules of epöphoron, under *ductule*.

**tu'buli galactoph'ori**, SYN lactiferous ducts, under *duct*.

**tu'buli lactif'eri**, SYN lactiferous ducts, under *duct*.

**tu'buli paro'ph'ori**, SYN ductuli paroöphori, under *ductulus*.

**t. rec'tus**, (1) SYN straight seminiferous tubule. (2) SYN straight seminiferous tubule.

**t. rena'lis contor'tus** [NA], SYN convoluted tubule of kidney.

**t. rena'lis rec'tus** [NA], SYN straight seminiferous tubule.

**t. seminif'erus contor'tus** [NA], SYN convoluted seminiferous tubule.

**t. seminif'erus rec'tus** [NA], SYN straight seminiferous tubule.

**t. transver'sus**, a tubular invagination of the sarcolemma of

skeletal or cardiac muscle fibers that surrounds myofibrils as the intermediate element of the triad; involved in transmitting the action potential from the sarcolemma to the interior of the myofibril.

**tu-bus**, pl. **tu-bi** (tū'būs, -bī). A tube or canal. [L.]

**t. digesto'rius**, SYN digestive tract.

**t. medulla'ris**, SYN central canal.

**t. vertebra'lis**, SYN vertebral canal.

**Tucker**, Ervin Alden, U.S. obstetrician, 1862-1902. SEE T. McLean forceps.

**tuft** (tūft). A cluster, clump, or bunch, as of hairs.

**enamel t.**, a group of structures representing defects in tooth mineralization that extend from the dentino-enamel junction into the enamel to about one-half its thickness.

**malpighian t.**, SYN glomerulus (2).

**synovial t.'s**, SYN synovial villi, under *villus*.

**tuft-sin** (tuf'sin). A tetrapeptide derived from the Fc region of an immunoglobulin. Tuftsin enhances macrophage functions. [Tufts University + -in]

**tug**, **tug-ging** (tūg, tūg'ing). A pulling or dragging movement or sensation.

**tracheal t.**, (1) a downward pull of the trachea, manifested by a downward movement of the thyroid cartilage, synchronous with the action of the heart and symptomatic of aneurysm of the aortic arch; the sign is elicited most easily by drawing the cricoid cartilage upward with the thumb and forefinger while the patient sits with head thrown back and mouth closed; (2) a jerky type of inspiration seen when the intercostal muscles and the sternocostal parts of the diaphragm are paralyzed by deep general anesthesia or muscle relaxants; due to the unopposed action of the crura pulling on the dome of the diaphragm and thence on the pericardium, lung roots, and tracheobronchial tree during each inspiration.

**tu-la-re-mia** (tū-lā-rē'mē-ā). A disease caused by *Francisella tularensis* and transmitted to humans from rodents through the bite of a deer fly, *Chrysops discalis*, and other bloodsucking insects; can also be acquired directly through the bite of an infected animal or through handling of an infected animal carcass; symptoms, similar to those of undulant fever and plague, consist of a prolonged intermittent or remittent fever and often swelling and suppuration of the lymph nodes draining the site of infection; rabbits are an important reservoir host. SYN deer-fly disease, deer-fly fever, Pahvant Valley fever, Pahvant Valley plague, rabbit fever. [Tulare, Lake and County, CA. + G. *haima*, blood]

**glandular t.**, t. with predominant lymph node infection as main manifestation.

**pulmonary t.**, t. affecting the lungs; tularemic pneumonia. SYN pulmonic t.

**pulmonic t.**, SYN pulmonary t.

**tulle gras** (tūl-grā'). A dressing for wounds, used chiefly in France, comprised of wide-mesh curtain net cut into squares and impregnated with soft paraffin (98 parts), balsam of Peru (1 part), and olive oil (1 part). [Fr. oily net]

**Tulp** (Tulpius), Nicholas (Nicolaus). Dutch anatomist, 1593-1674. SEE T.'s valve.

**tu-me-fa-cient** (tū-mē-fā'shent). Causing or tending to cause swelling. [L. *tume-facio*, to cause to swell, fr. *tumeo*, to swell]

**tu-me-fac-tion** (tū-mē-fak'shūn). 1. A swelling. SYN tumentia. 2. SYN tumescence. [see tumefaction]

**tu-me-fy** (tū-mē-fī). To swell or to cause to swell.

**tu-men-tia** (tū-men'shē-ā). SYN tumefaction (1). [L. fr. *tumeo*, to swell]

**tu-mes-cence** (tū-mēs'ens). The condition of being or becoming tumid. SYN tumefaction (2), tumescence. [L. *tumesco*, to begin to swell]

**tu-mes-cent** (tū-mēs'ent). Denoting tumescence. SYN tumescent.

**tu-mid** (tū'mid). Swollen, as by congestion, edema, hyperemia. SYN turgid. [L. *tumidus*]